35. The polynucleotide of claim 27, wherein the plurality of parental polynucleotide species encodes at least one Rubisco Form II subunit.

36. The polynucleotide of claim 27 further comprising a selectable marker gene which affords a means of selection when expressed in chloroplasts.

37. The polynucleotide of claim 36, wherein the sequence encoding a protein having Rubisco carboxylation activity and the selectable marker gene are flanked by an upstream flanking recombinogenic sequence having sufficient sequence identity to a chloroplast genome sequence to mediate efficient recombination and a downstream flanking recombinogenic sequence having sufficient sequence identity to a chloroplast genome sequence to mediate efficient recombination.

REMARKS

1. *Status of the claims*

Claims 1-9 and 20 are canceled without prejudice to subsequent revival. New claims 27-37 are added and currently under examination.

2. *Support for the Amendments*

Support for the amendments to the claims can be found throughout the specification, the drawings, and the claims as originally drafted. For example, support for new claim 27 can be found, e.g., in original claim 1 and on page 35, lines 19-20, describing carboxylation. Support for new claim 28 can be found, e.g., on page 35, lines 28-31, describing the carboxylation specificity factor. Support for new claims 29-32 can be found, e.g., on page 35, lines 30-31 of the specification. Support for new claim 33 can be found, e.g., on page 7, lines 3-14 of the specification. Support for new claim 34 can be found, e.g., on page 7, lines 15-26 of the specification. Support for new claim 35 can be found, e.g., on page 8, lines 15-21 of the specification. Support for new claim 36 can

be found, e.g., on page 24, line 30 to page 25, line 1 of the specification. Support for new claim 37 can be found, e.g., in original claim 15. No new matter is added in this Amendment.

3. Objection to hyperlinks in the Specification

The Examiner objected to hyperlinks in the specification. With entry of this Amendment, the hyperlinks are deleted. Accordingly, withdrawal of the objection is respectfully requested.

4. Objection to incorporation by reference

The Examiner alleges that essential material is incorporated into the specification by reference to foreign applications or patents or to non-issued U.S. patent applications. In particular, the Examiner objected to references in four sections of the specification: a) pages 39-40 of the specification, b) pages 47-48 of the specification, c) page 85 of the specification and d) page 86 of the specification.

While the Examiner has asserted that the above-described applications incorporate essential material, the Examiner has not provided any explanation for why the subject matter is essential. Applicants are willing to amend the application for essential material that is incorporated by reference. However, without further details regarding what the Examiner believes is essential, Applicants cannot determine what amendments are necessary. Moreover, the Examiner is reminded that MPEP § 608.01(p)(A) provides that essential material can be incorporated in pending U.S. applications.

5 Use of trademarks.

The Examiner requested that reference to trademarks such as TWEEN, NONIDET and TRITON be capitalized. Applicants have made such corrections per the Examiner's request. Accordingly, withdrawal of the rejection is respectfully requested.

6. Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-9 and 20 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not described in such a way as to enable those of skill in the art to make or use the claimed invention. Specifically, the Examiner argued that performance of the claimed methods require undue experimentation. Moreover, the Examiner stated that in the absence of Rubisco gene sequences for any and all plants described in the specification, the scope of the claims required an undue burden to perform the claimed invention.

To the extent the rejections apply to the new claims, Applicants respectfully traverse the rejection. The Examiner has not set forth a *prima facie* rejection under 35 U.S.C. § 112. Moreover, the present specification, combined with the state of the prior art, provides sufficient information necessary to carry out the claimed methods.

As articulated by the Federal Circuit, the proper test of enablement is "whether one skilled in the art could make or use the claimed invention from the disclosure in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 8 USPQ2d 1217 (Fed. Cir. 1988); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); MPEP § 2164.01. Indeed, according to the Federal Circuit in *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F. 2d 1367, 1385 (Fed. Cir. 1986), "a specification need not disclose what is well known in the art."

A. The Examiner fails to set forth a *prima facie* rejection

The rejection does not set forth a *prima facie* rejection under 35 U.S.C. § 112, first paragraph because the Examiner provides no basis to back up the assertions that those of skill in the art would not expect the claimed invention to function. As provided in *In re Marzocchi*, 439 F.2d 220, 224 (CCPA 1971),

> it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need

for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.
See, also MPEP § 2164.04.

In the rejection, the Examiner merely provides unsubstantiated statements regarding the amount of time necessary to perform the claimed methods, the unpredictability of the field of the invention and the state of the prior art. Moreover, the Examiner states that the amount of guidance provided by the specification is "severely limited" but does not explain what aspects of the claimed methods are allegedly not enabled. Although the Examiner states that the guidance in the application is prophetic, the Examiner provides no reasons why those of ordinary skill in the art would not expect the guidance to work as described in the specification. In the absence of concrete reasons explaining why the Examiner believes that the claimed methods would not work, the rejection fails to meet the minimum requirements set forth in the patent laws.

B. The specification provides sufficient guidance to perform the claimed methods

The Examiner implies that the material incorporated by reference in either foreign patent applications or unissued U.S. applications is required to enable the claimed invention. All of the references the Examiner alleges are improperly incorporated are directed to specific aspects of gene shuffling. The Examiner has not provided any specific explanation for why the material incorporated from foreign or non-issued U.S. applications is necessary to enable the present claims.

In fact, the application provides an extensive description of shuffling technologies. *See, e.g.*, page 40, line 27 to page 45, line 18. Moreover, the specification incorporates several issued patents describing gene shuffling on page 39, lines 1-12. Applicants submit that the specification provides sufficient detail to allow those of ordinary skill in the art to practice the full scope for the claimed invention. Therefore, withdrawal of the rejection is respectfully requested.

C. Rubisco sequences were available to the public as of the priority date of the present application

The Examiner appears to state that the claims are not fully enabled because the specification does not set forth every possible Rubisco sequence that could be recombined according to the methods of the invention. The Examiner argues that the Applicants have shifted the burden of enablement onto the public to isolate Rubisco sequences before the claimed methods can be practiced. In support of his position, the Examiner cites *Genentech v. Novo Nordisk A/S*, 42 USPQ2d 1001 (1997) and underlined the following quotation:

> However, when there is no disclosure of any specific starting material or any of the conditions under which a process can be carried out, undue experimentation is required; there is a failure to meet the enablement requirement that cannot be rectified by asserting that all of the disclosure related to the process is within the skill of the art.

In contrast to the position of the Examiner, the specification **does** provide starting materials, i.e., Rubisco sequences. For example, page 37, lines 9-26 of the specification refers to a number of references that contain different Rubisco sequences. Indeed, the specification states that over 1000 Rubisco sequences were known and described in Genbank prior to the filing date of the present application. Moreover, as one of the most studied enzymes in plant biology, it is unreasonable to suggest that Rubisco sequences from innumerable species were not available as of the priority date or that those of skill would have needed any more than a reference to know how to obtain such sequences. In light of the many Rubisco sequences available in the art at the time the application was filed, Applicants submit that the specification has met the requirement, articulated in *Genentech*, for the disclosure of necessary starting materials and conditions.

D. Summary

As discussed above, the rejection provides no objective reasons why those of skill in the art would not expect the claimed methods to function without undue

experimentation. Furthermore, the specification provides an adequate description of the methods and starting materials necessary to make and use the claimed invention, as required under the patent law. Accordingly, Applicants respectfully request withdrawal of the rejection.

7. ***Rejection under 35 U.S.C. § 112, second paragraph***

Claims 1-9 and 20 were rejected under 35 U.S.C. § 112, second paragraph because the Examiner alleged that numerous terms in the claims were indefinite. In light of cancellation of the claims, the rejections are moot.

Applicants note that the Examiner's concerns regarding "significantly higher" may also relate to the phrase "significantly enhanced" found in new claim 27. In light of the specification and the state of art at the time the application was filed, those of skill in the art would have found the phrase clear. Indeed, "significant" results in science relate to statistically significant results. In the context of the present claims, it is clear transformants are selected for expression of a protein with a carboxylation activity that is higher by a statistically significant factor relative to the activity of the protein encoded by the parental sequences. Therefore, the phrase "significantly enhanced" is clear.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Paragraph on page 28, lines 6-20:

"Physiological conditions" as used herein refers to temperature, pH, ionic strength, viscosity, and like biochemical parameters that are compatible with a viable plant organism or agricultural microorganism (e.g., Rhizobium, Agrobacterium, etc.), and/or that typically exist intracellularly in a viable cultured plant cell, particularly conditions existing in the nucleus of said cell. In general, in vitro physiological conditions can comprise 50-200 mM NaCl or KCl, pH 6.5-8.5, 20-45°C and 0.001-10 mM divalent cation (e.g., Mg^{++}, Ca^{++}); preferably about 150 mM NaCl or KCl, pH 7.2-7.6, 5 mM divalent cation, and often include 0.01-1.0 percent nonspecific protein (e.g., BSA). A non-ionic detergent (TWEEN ~~Tween~~, NONIDET-40 ~~NP-40~~, TRITON ~~Triton~~ X-100) can often be present, usually at about 0.001 to 2%, typically 0.05-0.2% (v/v). Particular aqueous conditions may be selected by the practitioner according to conventional methods. For general guidance, the following buffered aqueous conditions may be applicable: 10-250 mM NaCl, 5-50 mM Tris HCl, pH 5-8, with optional addition of divalent cation(s), metal chelators, nonionic detergents, membrane fractions, antifoam agents, and/or scintillants.

Paragraph on page 37, lines 9-26:

A variety of Rubisco gene and gene homologue sources are known and can be used in the recombination processes herein. For example, as noted, a variety of references herein describe such genes. For example, Croy, (ed.) (1993) Plant Molecular Biology Bios Scientific Publishers, Oxford, U.K. describe several Rubisco genes and sequence sources in public databases. Examples of public databases that include Rubisco sources include: Genbank~~: www.ncbi.nlm.nih.gov/genbank/~~; EMBL~~: www.ebi.ac.uk.embl/~~; as well as, e.g., the protein databank, Brookhaven Laboratories; the University of Wisconsin Biothechology Center, the DNA databank of Japan,

Laboratory of genetic Information Research, Misuina, Shizuda, Japan. As noted, over 1,000 different Rubisco homologues are available in Genbank alone. ~~In addition, specific internet sites which provide information regarding Rubisco include, e.g.,~~ ~~http://ss.tnaes.affrc.go.jp/pub/suzuki/rubisco.html;~~ ~~http://icdweb.cc.purdue.edu/~knollje/Rubisco.html;~~ ~~http://www.agron.missouri.edu/cgi-bin/sybgw_mdb/mdb3/Locus/114858;~~ ~~http://gdb.wehi.edu.au/scop/data/scop.1.004.037.001.000.000.html;~~ ~~http://www.blc.arizona.edu/courses/181gh/rick/photosynthesis/Calvin.html;~~ ~~http://www.tarweed.com/pgr/PGR98-207.html; and~~ ~~http://homepage.ruhr-uni-bochum.de/Marc.Sarie/rubisco3.html.~~

Paragraph bridging pages 72-73:

State-of-the-art commercial cyanofarming (aimed primarily on spirulina production for food) provides invaluable information and validated practical experience in such technology components as hardware and process design/engineering, biomass separation and drying, as well as in-depth insights into many other related technical problems (managing weed species, maintenance continuous year around cultivation). Sources describing cyanofarming include: Microalgae of Economic Potential by A. Richmond in CRC Handbook of Microalgal Mass Culture, 1986, CRC Press, Boca Raton, Florida;Microalgae: Organic Factories of the Future. Cyanotech Corp. 1998. and other information from Cyanotech~~: http://www.cyanotech.com~~; Spirulina: Environmental Advantages; Earthrise Farms, California~~: http://spirulina.com/SPPEnvironment.html~~; Jeeji Bai N (Poster Abstract, 1995) "Decentralized Arthrospira ("Spirulina") culture facility for income generation in rural areas" 1992 data. Shrii A.M.M Mudragappa Chettiar Research Centre, Tharamani, Madras 600113, India; Alkalophilic cyanobacteria: digests of Curds et al, 1986 and Finlay et al, 1987 ~~works http://www.nhm.ac.uk/zoology/extreme.html#alk~~; Spirulina - Production and Potential by Ripley D. Fox 1996. Pub. by Editions Edisud, La Calade, R.N.7 !3090 Aix-en-

provice, France~~; and information and references cited at http://www.cyanosite.bio.purdue.edu~~.